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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,622	02/13/2002	Raymond L. Houghton	210121.470C11	2478

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EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 05/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,622	HOUGHTON ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10-29-03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2-25-04 has been entered.

Response to Arguments

2. The rejection of claim 11 under 35 USC 102(e) and the rejection of claim 13 under 35 USC 112, 2nd have been withdrawn in response to Applicant's response filed 1-22-04.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

4. Claim 12 remains rejected and claim 13 is rejected under 35 U.S.C. 102(e) as being anticipated by Jager et al. (WO 01/47959 A2; see IDS received 4-18-02, reference AJ), for the reasons of record set forth in the Official Action mailed 8-25-2002.

Applicant's arguments filed 1-22-04 have been fully considered but they are not persuasive. Applicants argue that since claim 11 has been amended to recite that the 90% identity is to the full length of the polypeptide set forth in SEQ ID NO: 475, this amendment would obviate the pending rejection. The rejection of claim 11 was withdrawn, however the rejection of claim 12 is maintained since it is drawn to a method comprising the administration of an physiologically acceptable carrier or immunostimulant, and a polypeptide comprising at least 20

contiguous amino acids of the polypeptide set forth in SEQ ID NO: 475. Claim 13 is drawn to the method of claim 11, wherein said immunostimulant is selected from the group consisting of monophosphoryl lipid A, 3-de-O-acylated monophosphoryl lipid A, and a saponin alone or in combination.

SEQ ID NO: 16 of Jager et al. as disclosed in application 09/451,739 (priority date of 11-30-1999) comprises a sequence that is 99% identical to residues 338 to 847 of SEQ ID NO: 475 of the instant application. This polypeptide comprises at least 20 contiguous amino acids of the polypeptide set forth in SEQ ID NO: 475 of the instant application. Additionally, Jager et al. teach the immunotherapeutic treatment of a patient comprising administering the peptides disclosed by Jager et al. or immunoreactive portions thereof. The administration of said peptides may be administered in the form of a composition comprising standard pharmaceutical carriers, adjuvants, such as saponins, GM-CSF, and interleukins, see page 29, 2nd paragraph. Therefore, Jager et al. teach a method for stimulating an immune response by administration of a polypeptide comprising at least 20 contiguous amino acids of SEQ ID NO: 475, and further wherein said polypeptide is administered with an immunostimulant, wherein said immunostimulant is saponin.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 11 remains rejected and claims 12-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains

subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the Official action mailed 3-11-03 (Written Description). (In the Office Action mailed 8-25-03, the examiner mistakenly withdrew the rejection of claim 11 set forth in the Official action mailed 3-11-03.)

7. Applicant's arguments filed 6-05-03 were fully considered but they are not persuasive. Applicants traversed the instant rejection on the grounds that a sufficient and relevant identifying characteristic shared by members of the currently claimed genus is their % identify to the polypeptide set forth in SEQ ID NO: 475. Moreover, Applicants argue that the skilled artisan would understand and expect that an entire class of polypeptides structurally related to SEQ IDNO: 475, *e.g.*, sequences having at least 90% identify to SEQ ID NO: 475, would also be useful in the context of the Applicant's invention, despite the fact that they are not identical with the specific sequence of SEQ ID NO: 475.

The examiner agrees that there maybe polypeptides having 90% identity to SEQ ID NO: 475, which are useful in the context of the Applicant's invention. However, out of the broad genus of polypeptides which may have 90% identity to SEQ ID NO: 475, it is unclear how the skilled artisan, apart from further experimentation, would be able to predict which combination of modifications of SEQ ID NO: 475 that would produce a polypeptide of 90% would produce a polypeptide that is useful for producing an immune response in a patient for therapeutic purposes. There is no guidance as to which 10% of SEQ ID NO: 475 may be deleted, substituted or inserted, such that a polypeptide having at least 90% identity to SEQ ID NO: 475 is produced, wherein said polypeptide is useful for producing an immune response in a patient for therapeutic

purposes. Moreover, in regards to claim 12, Applicants do not provide sufficient guidance to the skilled artisan to predict which polypeptide comprising a 20 amino acid stretch of SEQ ID NO: 475 would produce a polypeptide useful in the claimed methods for producing an immune response in a patient for therapeutic purposes.

As stated in the prior Office Action, due to the limited structural information regarding what amino acid residues that may be deleted, substituted or inserted into the polypeptides according to the present invention, wherein said polypeptide retains at least 90% identity to SEQ ID NO: 475 or at least 20 contiguous amino acids of SEQ ID NO: 475 and maintains the ability to be used to stimulate an immune response in a patient, the level of unpredictability associated with protein structure and predicting protein function, and the lack of guidance thereof in the specification as filed, it is concluded that Applicant's disclosure is insufficient to adequately describe the genus of polypeptides encompassed by the claimed invention. Applicant's specification does not provide sufficient description for the broad genus of polypeptides encompassed by the instant claims since providing a means to isolate a compound cannot show possession. What is required is an actual description of the claimed invention, particularly by means of drawings or structural chemical formulas that show that the invention was complete at the time of filing of the claimed invention.

The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is required. Since the disclosure fails to describe the common attributes or characteristics that identify the members of the genus, and because the genus is highly variant, the disclosed sequence of SEQ ID NO: 475, alone is not sufficient to describe claimed genus.

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

8. Claims 11 remains rejected and claims 12-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record set forth in the Official Action mailed 3-11-03, and those reasons set forth below. (In the Office Action mailed 8-25-03, the examiner mistakenly withdrew the rejection of claim 11 set forth in the Official action mailed 3-11-03.)

Applicant's arguments filed 6-05-03 were fully considered but they are not persuasive. Applicants traversed the instant rejection on the grounds "that a skilled artisan would appreciate, particularly in light of the specification, that the claimed polypeptides could be used to generate a specific immune response against said polypeptide that is over-expressed on breast tumor tissues as compared to normal tissues. It is well accepted that the body's immune system normally keeps many cancers in check and that stimulation or re-stimulation of immune cells specific for antigens associated with cancer would be expected to lead to a therapeutic benefit. Thus, the specific immune response would preferentially target tissues that over-express the polypeptide (*i.e.*, tumor tissue). In this manner, the specific immune response generated would be effective in alleviating a cancer associated with the over-expression of the polypeptide of SEQ ID NO: 475."

First it is noted that Applicant's refer to prophetic teachings in the specification as filed as support for the enablement of the full scope of the claimed invention, specifically including the therapeutic treatment of breast cancer comprising the stimulation of an immune response in a patient comprising the administration of the polypeptides of the claimed invention. However, besides the fact that SEQ ID NO: 475 is over-expressed in breast tumor cells, there is no evidence that the expression of the polypeptides of the invention has a direct causal effect on the development of breast cancer, i.e. there is no elucidation of the actual function of the polypeptide within the breast cancer tissue. Moreover, there is no evidence that by stimulating the production of antibodies targeting this particular "antigen" would necessarily lead to the production of treatment effects specifically correlated with the treatment of breast cancer as it relates to the expression of the polypeptides of the present invention. Applicant's arguments are based solely upon prophetic teachings in the specification as filed.

It is not feasible to extrapolate the prophetic teachings of the specification to the practice of the full scope of the claimed invention due to the unpredictability associated with the behavior of drugs *in vitro* and their actual function in an animal *in vivo*. For example, Gura (Science, 1997, Vol. 278, pp. 1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile, and that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second paragraph). Due to the known unpredictability associated with drug therapy, specifically for the treatment of cancer, in the absence of actual experimental evidence, or even an actual working *in vitro* model, no one skilled in the art would

accept the assertion that the full scope of polypeptides encompassed by the instant claims would be specifically useful for the immuno-therapeutic treatment of breast cancer.

Hartwell et al. (Science, 1997, Vol. 278, pp. 1064-1068) teach that an effective chemotherapeutic must selectively kill tumor cells. However, as this reference suggests, most effective anticancer drugs have been discovered by serendipity and that the exact molecular alterations that provide selective tumor cell killing are unknown and that even understanding the detailed molecular mechanism by which a drug acts often provides little insight into why the treated tumor cell dies (bridging paragraph 1064-1065). Furthermore, Hartwell et al. teach that anti-tumor agents must accomplish several tasks to be effective. These tasks include, delivery into the circulation that supplies the tumor or metastatic promoter producing cells, interacts at the proper site of action, and must do so at a sufficient concentration and for a sufficient period of time.

The specification as filed does not teach one of skill in the art how to deliver the claimed polypeptides to a particular target tissue within an organism in order to produce a therapeutic result. In addition, variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy. The claimed formulations may be inactivated *in vivo* before producing a sufficient effect, for example by degradation, immunological activation or due to an inherently short half-life of the formulation (See Thompson, Medicinal Research Reviews, Vol. 21, No. 5, pages 412-449, 2001, especially pages 412-414). The specification does not provide sufficient guidance or instruction in regard to these issues and provides no working examples that would allow one skilled in the art to use the claimed compositions throughout the full scope of the claims without undue experimentation.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Epps-Ford, Ph.D.
Examiner
Art Unit 1635

JLE